Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Management of children with chronic wet cough and protracted bacterial bronchitis: CHEST guideline and Expert Panel report.

Bibliographic Source(s)

Chang AB, Oppenheimer JJ, Weinberger MM, Rubin BK, Grant CC, Weir K, Irwin RS, CHEST Expert Cough Panel. Management of children with chronic wet cough and protracted bacterial bronchitis: CHEST guideline and Expert Panel report. Chest. 2017 Apr;151(4):884-90. [33 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Chang AB, Glomb WB. Guidelines for evaluating chronic cough in pediatrics: ACCP evidence-based clinical practice guidelines. Chest. 2006 Jan;129(1 Suppl):260S-83S. [272 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

= Poor = Fair = Good = Very Good = Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source
	Disclosure and Management of Financial Conflict of Interests

	Guideline Development Group Composition
YES	Multidisciplinary Group
YES	Methodologist Involvement
▮▮▮▮▯	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
▮▮▮▮▮	Search Strategy
▮▮▮▮▮	Study Selection
▮▮▮▮▮	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
▮▮▮▮▯	Grading the Quality or Strength of Evidence
▮▮▯▯▯	Benefits and Harms of Recommendations
▮▮▮▮▯	Evidence Summary Supporting Recommendations
▮▮▮▮▮	Rating the Strength of Recommendations
▮▮▮▮▮	Specific and Unambiguous Articulation of Recommendations
▮▯▯▯▯	External Review
▮▮▮▮▮	Updating

Recommendations

Major Recommendations

The grades of recommendation (1A–2C, consensus-based [CB]) and the approach to rating the quality of evidence are defined at the end of the "Major Recommendations" field.

> For children aged ≤14 years with chronic (> 4 weeks' duration) wet or productive cough unrelated to an underlying disease and without any specific cough pointers (e.g., coughing with feeding, digital clubbing), the Expert Panel recommends that children receive 2 weeks of antibiotics targeted to common respiratory bacteria (*Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis*) and local antibiotic sensitivities (Grade 1A).
> For children aged ≤14 years with chronic wet or productive cough unrelated to an underlying disease and without any specific cough pointers (e.g., coughing with feeding, digital clubbing) and whose cough resolves within 2 weeks of treatment with antibiotics targeted to local antibiotic sensitivities, the Expert Panel recommends that the diagnosis of protracted bacterial bronchitis (PBB) be made (Grade 1C).
> For children aged ≤14 years with PBB with lower airway (bronchoalveolar lavage or sputum) confirmation of clinically important density of respiratory bacteria (≥10^4 cfu/ml), the Expert Panel recommends that the term "microbiologically-based-PBB" (or PBB-micro) be used to differentiate it

from clinically-based-PBB (PBB without lower airway bacteria confirmation) (Grade 1C).

For children aged ≤14 years with chronic wet or productive cough unrelated to an underlying disease and without any specific cough pointers (e.g., coughing with feeding, digital clubbing) when the wet cough persists after 2 weeks of appropriate antibiotics, the Expert Panel recommends treatment with an additional 2 weeks of the appropriate antibiotic(s) (Grade 1C).

For children aged ≤14 years with chronic wet or productive cough unrelated to an underlying disease and without any specific cough pointers (e.g., coughing with feeding, digital clubbing), when the wet cough persists after 4 weeks of appropriate antibiotics, the Expert Panel suggests that further investigations (e.g., flexible bronchoscopy with quantitative cultures and sensitivities with or without chest computed tomography) be undertaken (Grade 2B).

For children aged ≤14 years with chronic wet or productive cough unrelated to an underlying disease and with specific cough pointers (e.g., coughing with feeding, digital clubbing), the Expert Panel recommends that further investigations (e.g., flexible bronchoscopy and/or chest computed tomography, assessment for aspiration and/or evaluation of immunologic competency) be undertaken to assess for an underlying disease (Grade 1B).

For children aged ≤14 years with chronic wet or productive cough unrelated to an underlying disease and without any specific cough pointers (e.g., coughing with feeding, digital clubbing), the Expert Panel suggests that randomized controlled trials on the efficacy of different durations of antibiotics be undertaken in various clinical settings (particularly in primary care) to determine its influence on the number to treat and recurrence. When doing so, the Expert Panel suggests that validated cough outcomes and a-priori definitions be used (Ungraded, Consensus Based Statement).

Definitions

American College of Chest Physicians (CHEST) Grading System

Grade of Recommendation	Balance of Benefit vs. Risk and Burdens (Strength of the Recommendation: Level 1 or 2)	Methodologic Strength of Supporting Evidence (Quality of Body of Evidence: A, B, C, or CB)	Implications
Graded evidence-based guideline recommendations			
Strong recommendation, high-quality evidence (1A)	Benefits clearly outweigh risk and burdens or vice versa	Consistent evidence from randomized controlled trials (RCTs) without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect.
Strong recommendation, moderate-quality evidence (1B)	Benefits clearly outweigh risk and burdens or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances. Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate.
Strong recommendation, low- or very-low-quality evidence (1C)	Benefits clearly outweigh risk and burdens or vice versa	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate.
Weak recommendation, high-quality evidence (2A)	Benefits closely balanced with risks and burden	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from	The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change confidence in the

Grade of Recommendation	Balance of Benefit vs Risk and Burdens (Strength of the Recommendation: Level 1 or 2)	Methodologic Strength of Supporting Evidence (Quality of Body of Evidence: A, B, C, or CB)	Implications
Weak recommendation, moderate-quality evidence (2B)	Benefits closely balanced with risks and burden	observational studies Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies	estimate of effect Best action may differ depending on circumstances or patient's or societal values. Higher-quality research may well have an important impact on confidence in the estimate of effect and may change the estimate.
Weak recommendation, low- or very-low-quality evidence (2C)	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Evidence for at least one critical outcome from observational studies, case series, or RCTs, with serious flaws or indirect evidence	Other alternatives may be equally reasonable. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate.
Nongraded consensus-based suggestions			
Consensus-based (CB)	Uncertainty due to lack of evidence but expert opinion that benefits outweigh risk and burdens or vice versa	Insufficient evidence for a graded recommendation	Future research may well have an important impact on confidence in the estimate of effect and may change the estimate.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Chronic (>4 weeks' duration) wet or productive cough
- Protracted bacterial bronchitis

Guideline Category

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Pediatrics

Pulmonary Medicine

Intended Users

Physicians

Guideline Objective(s)

To formulate recommendations based on systematic reviews related to the management of chronic wet cough in children (aged ≤14 years) based on two key questions: (1) how effective are antibiotics in improving the resolution of cough? If so, what antibiotic should be used and for how long? and (2) when should children be referred for further investigations?

Target Population

Children aged ≤14 years with chronic (>4 weeks' duration) wet or productive cough

Note: Premature infants and neonates are excluded from these recommendations.

Interventions and Practices Considered

1. Antibiotics targeted to common respiratory bacteria and local antibiotic sensitivities
2. Diagnosing protracted bacterial bronchitis (PBB) based on specified criteria
3. Use of specific terminology to differentiate microbiologically-based-PBB and clinically-based-PBB
4. Further investigations
    - Flexible bronchoscopy
    - Chest computed tomography (CT) scans
    - Assessment for aspiration
    - Evaluation of immunologic competency
5. Randomized controlled trials

Major Outcomes Considered

- Etiology of cough
- Resolution of cough
- Effectiveness of antibiotic treatment

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The systematic reviews were conducted based on the protocol established by selected members of the American College of Chest Physicians (CHEST) expert cough panel. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement was used for reporting.

The searches for both questions were conducted by librarians from the University of Massachusetts Medical School between July 19, 2015, and July 27, 2015, using the search strategies outlined in e-Table 1 and e-Table 2 (see the systematic review [see the "Availability of Companion Documents" field]). For the CHEST cough guidelines, it was determined a priori that the age cutoff for pediatric and adult components was 14 years. However, to ensure that all relevant studies were captured, the search filter

included studies in subjects up to 18 years of age. The reviewers included only studies published in English. Duplicates found between Scopus and PubMed searches were identified and removed by the librarians before sending the abstracts to the two authors who reviewed the abstracts.

The two reviewers independently reviewed all abstracts and agreed on which full-text articles to retrieve to assess for potentially eligible studies. It was planned that disagreements that could not be resolved by consensus would have been adjudicated by a third reviewer.

See the Online Supplement for additional information on study selection criteria and search strategy (see the "Availability of Companion Documents" field).

Number of Source Documents

- Key Question 1: 15 studies included in current systematic review
- Key Question 2: 17 studies included in current systematic review

See Figures 1 and 2 in the systematic review (see the "Availability of Companion Documents" field) for the study selection process.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

The quality of evidence is based on the five domains of risk of bias, inconsistency, indirectness, reporting bias, and imprecision. The quality of evidence (i.e., the confidence in estimates) is rated as high (A), moderate (B), low, or very low (C) (see the "Rating Scheme for the Strength of the Recommendations" field).

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

For randomized controlled trials (RCTs), both reviewers independently assessed the risk of bias criteria by using measures in Cochrane reviews. The criteria used were: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), and selective reporting (reporting bias). For cohort studies, data were extracted by a single author and checked by a second author. In cohort studies, the study's setting, number enrolled and completing the study, inclusion and exclusion criteria, and main results related to the respective key questions (KQs) are reported (Tables 1-4 in the systematic review [see the "Availability of Companion Documents" field]). For KQ2, the reviewers also described studies that reported on the association between duration of chronic wet cough and outcomes (Table 5) and mechanistic or pathobiology studies (Table 6).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

The authors used a standard method as previously used by panel members: "The methodology used by the CHEST Guideline Oversight Committee to select the Expert Cough Panel Chair and the international panel of experts, perform the synthesis of the evidence and develop the recommendations and suggestions has been published. Key questions and parameters of eligibility were developed for this topic. Existing guidelines, systematic reviews, and primary studies were assessed for relevance and quality, and were used to support the evidence-based graded recommendations or suggestions. A highly structured consensus-based Delphi approach was employed to provide expert advice on all guidance statements. The total number of eligible voters for each guideline statement varied based on the number of managed individuals recused from voting on any particular statements because of their potential conflicts of interest. Transparency of process was documented." In line with the American College of Chest Physicians (CHEST) guideline methodology (see the "Availability of Companion Documents" field), a comprehensive, systematic review of the literature was undertaken to provide the evidence base for recommendations outlined here.

Guideline Framework

As previously described, "the American College of Chest Physicians has adopted the GRADE framework (the Grading of Recommendations Assessment, Development and Evaluation). This framework separates the process of rating the quality of evidence from that of determining the strength of recommendation. The quality of evidence is based on the five domains of risk of bias, inconsistency, indirectness, reporting bias, and imprecision. The quality of evidence (i.e., the confidence in estimates) is rated as high (A), moderate (B), low, or very low (C). The strength of recommendation is determined based on the quality of evidence, balance of benefits and harms, patients' values and preferences and availability of resources." Recommendations can be strong vs weak or Grade 1 vs. 2 or ungraded.

State of the Available Evidence

The systematic review identified high-quality evidence to support some recommendations but not all. Where there was insufficient evidence for diagnosis and management recommendations, the panel heavily considered patient values, preferences, ease and cost of tests, and availability of potential therapies. The panel also made several suggestions for future research.

Rating Scheme for the Strength of the Recommendations

American College of Chest Physicians (CHEST) Grading System

Grade of Recommendation	Balance of Benefit vs. Risk and Burdens (Strength of the Recommendation: Level 1 or 2)	Methodologic Strength of Supporting Evidence (Quality of Body of Evidence: A, B, C, or CB)	Implications
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Strong recommendation, moderate-quality evidence (1B)	Benefits clearly outweigh risk and burdens or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence	Recommendation can apply to most patients in most circumstances. Higher-quality research may well have an important impact on confidence in the estimate of effect and

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Strong recommendation, low- or very-low-quality evidence (1C)	Benefits clearly outweigh risk and burdens or vice versa	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances. Higher-quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate.
Weak recommendation, high-quality evidence (2A)	Benefits closely balanced with risks and burden	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient's or societal values. Further research is very unlikely to change confidence in the estimate of effect.
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Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Review Process

After the Cough Executive Committee provided final approval, the NetWorks, Guidelines Oversight Committee (GOC), and Board of Regents disseminated manuscripts and supporting documentation for review. The CHEST NetWorks of interested members, in the areas of Airways Disorders, Allied Health, Clinical Pulmonary Medicine, Pediatric Chest Medicine, Pulmonary Physiology Function and Rehabilitation, and Respiratory Care, reviewed the content of the manuscripts. Members from the CHEST Board of Regents and GOC reviewed both content and methods, including consistency, accuracy, and completeness. The *CHEST* journal peer review process overlapped with the later rounds of these reviews. All ideas for modification were marked as mandatory or suggested, responded to or justified, and tracked

through the multiple rounds of review. The CHEST Presidential line of succession provided the final approval allowing submission to the journal.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

The efficacy of antibiotic treatment for resolving chronic wet cough in children was evident from three randomized controlled trials (RCTs) in which the forest plot from the combined RCT data showed a clear benefit (number needed to treat for benefit by end of study was 3 [95% confidence interval [CI], 2.0-4.3]). Consistent with RCT data, all other studies included in the systematic review reported benefit irrespective of the study design (e.g., prospective and retrospective studies).

Potential Harms

Not stated

Qualifying Statements

Qualifying Statements

American College of Chest Physicians (CHEST) guidelines are intended for general information only, are not medical advice, and do not replace professional medical care and physician advice, which always should be sought for any medical condition. The complete disclaimer for this guideline can be accessed at http://www.chestnet.org/Guidelines-and-Resources .

Implementation of the Guideline

Description of Implementation Strategy

Dissemination

After publication, the guidelines were promoted to a wide audience of physicians, other health-care providers, and the public through multiple avenues. Press releases were prepared for both the lay and medical media, with major outreach efforts to all relevant print, broadcast, and Internet media. Panelists located in various large media markets were identified as potential spokespersons for interviews. Social media promotion was facilitated over Twitter, Facebook, CHEST e-Communities, internal and external blogs, and other communication routes. Blast communications were sent to CHEST members with links to the publication and postings on CHEST's Web site.

In addition to publication in *CHEST*, other derivative products were prepared to help with implementation, including slide sets, algorithms, and other clinical tools. These derivative products are posted on the CHEST Web site and will be made available in CHEST Guidelines. CHEST Guidelines will be the repository for the most current recommendations and suggestions from all CHEST guidelines, consensus statements, and hybrid documents. This online repository will also house a collection of related resources.

Associations that appointed representatives earlier in the process were asked to consider endorsing the approved guidelines for listing in the final publication. These organizations were requested to help promote the publication to their memberships through newsletters, Web sites, and other means.

Implementation Tools

Mobile Device Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Chang AB, Oppenheimer JJ, Weinberger MM, Rubin BK, Grant CC, Weir K, Irwin RS, CHEST Expert Cough Panel. Management of children with chronic wet cough and protracted bacterial bronchitis: CHEST guideline and Expert Panel report. Chest. 2017 Apr;151(4):884-90. [33 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 Apr

Guideline Developer(s)

American College of Chest Physicians - Medical Specialty Society

Source(s) of Funding

American College of Chest Physicians

Guideline Committee

American College of Chest Physicians (CHEST) Expert Cough Panel

Composition of Group That Authored the Guideline

Authors: Anne B. Chang, MBBS, PhD, MPH; John J. Oppenheimer, MD; Miles M. Weinberger, MD, FCCP; Bruce K. Rubin, MD; Cameron C. Grant, MBChB, PhD; Kelly Weir, BSpThy, MSpPath, PhD, CPSP; Richard S. Irwin, MD, Master FCCP

Financial Disclosures/Conflicts of Interest

Conflict-of-Interest Reviews

For practitioners to adhere to guideline or consensus statement recommendations, they must have confidence that the convened experts represent all relevant stakeholders and do not harbor biases that might influence the discussions and resulting clinical recommendations or suggestions. This is even more important when guidance includes consensus of a panel of experts. The chair of this project was vetted and determined to be free of conflicts of interest (COIs). The Guidelines Oversight Committee (GOC) Policies and Procedures Subcommittee and the full GOC, in accordance with explicit rules regarding COI and expertise, carefully reviewed all nominees. Greater explanations of these and other evidence-based processes are published separately. The panel is predominantly free of relevant COIs. A few individuals with moderate conflicts, whose expertise was highly valued and who could not be easily replaced, were selected. These panelists were given individualized management plans and restricted from writing and voting on clinical content areas related to current conflicts and participation in future activities that could be perceived as conflicts.

Financial/Nonfinancial Disclosures

The authors have reported to *CHEST* the following: A. B. C. has an intellectual conflict of interest, being an author of several of the papers included in this review. A. B. C. is supported by an Australian National Health Medical Research Council (NHMRC) practitioner fellowship (grant 1058213) and holds multiple grants awarded from the NHMRC related to diseases associated with pediatric cough. The views expressed in this publication are those of the authors and do not reflect the views of the NHMRC. J. J. O. declares the following: Board of Directors, American Board of Allergy and Immunology; Associate Editor, Annals of Allergy and Allergy Watch; reviewer, Up to Date; clinical research, Boehringer Ingelheim, AstraZeneca, Glaxo, MedImmune, and Novartis; adjudication committee, AstraZeneca and Novartis; data and safety monitoring board, The Ohio State University; and consultant, Glaxo, Myelin, Church and Dwight, and Meda. R. S. I. reports that he has no financial or intellectual conflicts of interest regarding the content of this manuscript. Moreover, although R. S. I. is the Editor-in-Chief of CHEST, the review and all editorial decisions regarding this manuscript were independently made by others. None declared (M. M. W., B. K. R., C. C. G., K. W.).

Guideline Endorser(s)

American Academy of Allergy, Asthma and Immunology - Medical Specialty Society

American Association for Respiratory Care - Professional Association

American Thoracic Society - Medical Specialty Society

Asian Pacific Society of Respirology - Disease Specific Society

Irish Thoracic Society - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

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This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the CHEST Journal Web site. Also available to CHEST Journal subscribers through the CHEST app for iOS and Android.

Availability of Companion Documents

The following are available:

Chang AB, Oppenheimer JJ, Weinberger M, Rubin BK, Irwin RS. Children with chronic wet or productive cough - treatment and investigations: a systematic review. Chest. 2016 Jan;149(1):120-42. Available from the CHEST Journal Web site.

Children with chronic wet or productive cough - treatment and investigations: a systematic review. Online supplement. Chest. 2016 Jan. 5 p. Available from the CHEST Journal Web site.

Lewis SZ, Diekemper RL, French CT, Gold PM, Irwin RS. Methodologies for the development of the management of cough: CHEST guideline and Expert Panel report. Chest. 2014 Jul;146(5):1395-402. Available from the CHEST Journal Web site.

Lewis SZ, Diekemper RL, Ornelas J, Casey KR. Methodologies for the development of CHEST guidelines and Expert Panel reports. Chest. 2014 Jul;146(1):182-92. Available from the CHEST Journal Web site.

Irwin RS, French CT, Lewis SZ, Diekemper RL, Gold PM. Overview of the management of cough: CHEST guideline and Expert Panel report. Chest. 2014(4):885-9. Available from the CHEST Journal Web site.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on May 4, 2006. The information was verified by the guideline developer on June 5, 2006. This summary was updated by ECRI Institute on October 4, 2017. The guideline developer agreed to not review the content.

This NEATS assessment was completed by ECRI Institute on October 4, 2017. The guideline developer agreed to not review the content.

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